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(71) Applicant *(for all designated States except US)*: **FIRST SCIENTIFIC, INC.** [US/US]; Suite 200, 1877 West 2800 South, Ogden, UT 84401 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: **WALKER, Edward, B.** [US/US]; 3655 Mount Ogden Drive, Ogden, UT 84403 (US).

(74) Agents: **BOND, Laurence, B.** et al.; Trask Britt, P.O. Box 2550, Salt Lake City, UT 84110 (US).

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(54) Title: ANTIMICROBIAL TOPICAL COMPOSITION AND METHODS

(57) Abstract: An antimicrobial topical composition including a quatenary ammonium compound in the antimicrobial component thereof. The quatenary ammonium compound may be benzethonium chloride. Benzethonium may constitute up to about 1% of the weight of the topical composition. The topical composition also has water and a cationic surfactant component for cleansing and to emulsify any hydrophobic components in the water. The topical composition my be a lotion that includes a stable, creamy emulsion of the hydrophobic component in the water or a more dilute liquid emulsion. The invention also includes wipe sheets wetted or impregnated with the topical composition. The topical composition can be applied to the skin and left thereon or removed from the

ANTIMICROBIAL TOPICAL COMPOSITION AND METHODS

TECHNICAL FIELD

The present invention relates to an antimicrobial topical composition including a quaternary ammonium compound as the active antimicrobial component thereof. Particularly, the present invention relates to topical compositions with an antimicrobial component including benzethonium chloride, a cationic surfactant component for cleansing the skin and for emulsifying the hydrophobic components of the topical composition, and substantially no low molecular weight alcohols. The present invention also relates to products including the antimicrobial topical composition and to methods of making and using the antimicrobial topical composition.

BACKGROUND ART

Antimicrobial topical compositions are commonly used by healthcare personnel, in biological laboratories, and in other settings where the elimination of bacteria from the skin is desired. In the healthcare and laboratory settings, personnel are encouraged to wash their hands frequently, often several times each day, in order to prevent the transfer of microorganisms and to reduce the likelihood of infection or contamination by microorganisms.

Conventionally, antimicrobial topical compositions have taken the form of soaps. Other types of antimicrobial topical compositions, such as lotions, gels, and foams, have also been used. In order to effectively reduce the number of bacteria and other microorganisms on skin to acceptable levels, these antimicrobial topical compositions are formulated with sufficient concentrations of antimicrobial agents to kill bacteria on contact or during exposure times of a few seconds.

For example, many of antimicrobial topical compositions include large amounts of low molecular weight alcohols (i.e., alcohols having up to four carbon atoms), such as ethanol or isopropyl alcohol. The low molecular weight alcohol in these compositions is effective in killing bacteria, but tends to dry the skin.

Other conventional antimicrobial topical compositions include iodine, triclosan, parachlorometaxylenol ("PCMX"), chlorhexidine gluconate ("CHG"), or hexachloropitine as the active antimicrobial components thereof. Like alcohol, with

frequent use, antimicrobial topical compositions containing each of these antimicrobial components may also cause dry skin or otherwise irritate the skin.

Some antimicrobial topical compositions include other antimicrobial components. For example, quaternary ammonium compounds are used in the antimicrobial topical compositions disclosed in United States Patent 5,244,666 (hereinafter "the '666 Patent"), issued to Jack C. Murley on September 14, 1993; United States Patents 5,492,932 (hereinafter "the '932 Patent") and 5,767,163 (hereinafter "the '163 Patent"), issued to Ruth B. Kundsin on February 20, 1996, and June 16, 1998, respectively; and European patent 0 389 648 B1.

Quaternary ammonium compounds are used as an antimicrobial component of some of these compositions, and as a cationic surfactant in others. Since quaternary ammonium compounds are surfactants, if used in a topical composition in high concentrations, quaternary ammonium compounds may remove oils and, thus, moisture, from skin upon rinsing the topical composition from the skin. High concentrations of quaternary ammonium compounds may also irritate the skin.

The '666 Patent discloses a composition that may be used as pre-operative skin scrub or as a topical disinfectant. The composition of the '666 Patent has two antimicrobial components, a quaternary ammonium compound and a substituted phenolic compound. The quaternary ammonium compound is described as a phosphate imidazolinium or phosphate quaternary compound. The composition contains approximately 3% by weight of each of the quaternary ammonium compound and the substituted phenolic compound. The use of such a high concentration of a quaternary ammonium compound as a surgical scrub is somewhat undesirable in that, upon scrubbing the skin, the quaternary ammonium compound can emulsify oils in the skin, which are subsequently removed from the skin when the surgical scrub is rinsed from the skin. Thus, the composition disclosed in the '666 Patent may cause dry skin or may otherwise irritate the skin.

The '932 and '163 Patents each disclose a lubricating, germicidal topical composition that includes isopropyl alcohol, cetyl alcohol, glycolic acid, and a quaternary ammonium salt such as benzalkonium chloride. Benzalkonium chloride makes up about 0.017% to about 0.26% of the weight of the composition, while isopropyl alcohol constitutes about 90-98% of the weight of the composition.

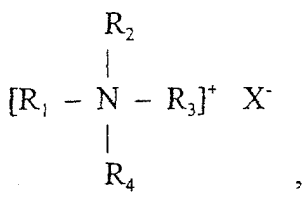
The '932 and '163 Patents each state that the isopropyl alcohol and benzalkonium chloride of the composition impart antimicrobial properties to the composition. The combination of benzalkonium chloride and isopropyl alcohol is disclosed to provide substantially instantaneous disinfection on contact and also provides a synergistic effect which increases each ingredient's germicidal activity. The composition also contains cetyl alcohol and a lubricating amount of glycolic acid to prevent drying of the skin by the isopropyl alcohol. When applied to the skin, the dried composition provides a persistent residual film until washed off with conventional soap and water. The composition is disclosed to be beneficial in combination with a hand wash containing a detergent or antiseptic. Therefore, the composition of the '932 and '163 Patents cannot be used alone as a soap. In addition, the germicidal residue can last up to one year on a hard surface if left undisturbed.

Each of these compositions are relatively watery solutions.

European patent application 0 389 648 B1 discloses a composition that is useful for decontaminating or disinfecting purposes and that may be metered by a soap dispenser. The composition includes benzalkonium chloride as a cationic surfactant. Benzalkonium chloride constitutes at least about 5% of the composition, by weight. The composition has antimicrobial properties. As stated previously, however, the use of such a high concentration of cationic surfactants can dry or irritate the skin, making the composition disclosed in European patent application 0 389 648 B1 somewhat undesirable.

Lotions and creams that include quaternary ammonium compounds are also known. Typically, lotions and creams are either water-in-oil or oil-in-water emulsions that have at least about 25% oils, or hydrophobic materials. Conventional creams and lotions have such high oil contents to facilitate stability of the emulsions and to impart the creams and lotions with cream, smooth textures. Examples of creamy, stable emulsion topical compositions that include quaternary ammonium compounds are disclosed in United States Patents 5,759,557 (hereinafter "the '557 Patent") and 5,759,558 (hereinafter "the '558 Patent"), both issued to Howard Epstein et al. on June 2, 1998; and United States Patent 5,869,061 (hereinafter "the '061 Patent"), issued to Bettie Sue Brugh on February 9, 1999.

The '557 and '558 Patents disclose moisturizing creams or lotions that are oil-in-water emulsions and that contain a quaternary ammonium compound of the general formula:



where R_1 and R_2 are each long chain, substantially linear alkyl groups having from about 16 to about 22 carbon atoms, R_3 and R_4 are each alkyl groups having from about 1 to about 3 carbon atoms, and X is a salt-forming anion (i.e., negatively charged ion) when the quaternary ammonium compound is dissolved in water. Quaternary ammonium compounds make up about 3% to about 8% of the weight of the moisturizing cream or lotion. The '557 and '558 Patents each provide that these quaternary ammonium compounds are useful as moisturizers due to their hard, waxy, and non-sticky characteristics. The composition described in the '557 and '558 Patents is not disclosed to be useful as a soap.

The '061 Patent discloses a protective hand lotion consisting of aloe vera gel, vitamin E gel, petroleum jelly, and an emulsion component composed of water and various hydrophilic and hydrophobic ingredients. The emulsion component, which makes up about 70 to about 88 percent of the weight of the lotion, includes a quaternary ammonium salt, dimethyl distearyl ammonium chloride, as the emulsifier. The quaternary ammonium salt makes up about 4% of the weight of the emulsion component. The lotion of the '061 Patent does not rinse off of the skin, but rather acts as a protective barrier to provide protection against normal handwashing procedures with soap and water for up to three handwashings.

The topical compositions disclosed in the '557, '558, and '061 Patents are creams or lotions that are not intended to be rinsed from the skin. None of these patents discloses that the quaternary ammonium compounds thereof are useful as antimicrobials.

Moreover, the topical compositions disclosed in each of the '557, '558, and '061 Patents has a relatively high content of hydrophobic components. The hydrophobic components of the topical compositions disclosed in the '061 Patent make

up at least about 25% of the weight of the topical compositions. The embodiment disclosed in EXAMPLE 1 includes JOHNSON'S baby lotion, which is known in the art to include at least about 25% mineral oil and other hydrophobic components. Of the remaining ingredients of the composition, petroleum jelly alone makes up about 28% of the weight thereof. Similarly, the embodiment of the topical composition disclosed in EXAMPLE 2 has about 28% petroleum jelly, by weight. As a result of the high content of hydrophobic components in these topical compositions, the antimicrobial properties of the quaternary ammonium compounds in these topical compositions may be diminished or completely masked.

Thus, the art does not teach an antimicrobial topical composition that has a quaternary ammonium compound as the antimicrobial component thereof in an amount that will not irritate or dry the skin and moisturizers that will not significantly diminish the antimicrobial activity of the antimicrobial component.

DISCLOSURE OF INVENTION

The present invention includes a topical composition, such as a lotion or a spray. A topical composition incorporating teachings of the present invention is substantially free of low molecular weight alcohols (i.e., alcohols, such as methanol, ethanol, propyl alcohols, and butyl alcohols, that include from 1 to 4 carbon atoms) and includes a quaternary ammonium compound as an antimicrobial agent. The topical composition also includes a hydrophobic (i.e., "fat hating") component and a cationic surfactant component for cleansing skin and emulsifying the hydrophobic component in water. A topical composition according to the present invention may also include other components, such as moisturizing agents, therapeutic agents, medicinal agents, fragrances, botanical extracts, preservatives, and pH adjusting agents.

As stated above, low molecular weight alcohols, which are commonly employed as antimicrobial ingredients of topical compositions, can remove moisture-providing oils from the skin. Low molecular weight alcohols may also cause pain in open skin wounds. Accordingly, the topical composition of the present invention is substantially free of low molecular weight alcohols.

The antimicrobial component of the topical composition of the present invention preferably includes a quaternary ammonium compound that kills

microorganisms by disrupting, or forming holes in, the biological membranes of many microorganisms. When the membranes of many microorganisms are disrupted, the various parts of the microorganism leak out or harmful materials enter the membrane, effectively killing the microorganism. The quaternary ammonium compound known in the art as benzethonium chloride is preferred for use in the topical composition of present invention.

Preferably, the antimicrobial component of the topical composition includes a quaternary ammonium compound that, when diluted to a 1% solution, will kill microorganisms such as *E. coli*, *Staphylococcus* species, and *Pseudomonas* species or at least hold these microorganisms at stasis, or prevent significant growth of the number of microorganisms. The quaternary ammonium compound of the antimicrobial component of the topical composition also preferably "kills" viruses, such as the herpes simplex viruses (type-1 and type-2) (HSV-1 and HSV-2) and rhinovirus. For example, the quaternary ammonium compound of the antimicrobial component may make up about 1% of the weight of the topical composition. Preferably, the quaternary ammonium compound makes up about 0.1 to about 0.2% of the total weight of the topical composition.

Examples of hydrophobic materials that can be used in the topical composition of the present invention include, without limitation, fragrances and botanical oils. Hydrophobic materials that moisturize, protect, act as emollients, or otherwise therapeutically benefit the skin are another example of hydrophobic materials that can be employed as the hydrophobic component of the topical composition according to the present invention. Water soluble moisturizers and emollients may also be employed.

When moisturizers or emollients are employed in the topical composition of the present invention, the moisturizers or emollients employed or the proportions in which the moisturizers or emollients are employed preferably do not significantly diminish the antimicrobial activity of the quaternary ammonium compound of the antimicrobial component of the topical composition. Exemplary moisturizers and emollients that can be included in the topical composition include, without limitation, glycerol, petrolatum, mineral oil, and silicone oils.

Hydrophobic (i.e., "water hating") components of the topical composition can be emulsified, or suspended, in the water of the topical composition with surfactants,

which are also commonly referred to in the art as emulsifiers. Since quaternary ammonium compounds are cationic, or positively charged ionic, compounds, anionic substances, such as anionic surfactants, may diminish the antimicrobial and other properties of the quaternary ammonium compound. The surfactants that are used in the topical composition to emulsify the hydrophobic components thereof are preferably cationic surfactants.

A cationic surfactant has a hydrophilic (i.e., "water loving") head and a lipophilic (i.e., "fat loving") tail. When mixed with water and a hydrophobic material, such as a silicone oil, to form an oil-in-water emulsion, the lipophilic tails of a number of surfactant molecules implant themselves into a quantity of the hydrophobic material to form a surfactant-coated droplet of the hydrophobic material, or micelle. The positively charged portion of a cationic surfactant is the hydrophilic portion thereof, which faces away from the hydrophobic material and toward the water, or aqueous, portion of the emulsion. As micelles are removed from an aqueous environment, such as the water of the topical composition, by evaporating the water or otherwise, the micelles release the droplet hydrophobic material.

Preferably, one or more quaternary ammonium compounds are employed as a cationic surfactant component of the topical composition of the present invention. The surfactant or surfactants of the cationic surfactant component are preferably used in the topical composition of the present invention in concentrations that are not irritating to tissues of the body, such as skin.

The topical composition may also include a preservative component of one or more preservatives. Preferably, the topical composition includes a blend of two or more preservatives.

According to another aspect of the present invention, a method for manufacturing the topical composition includes mixing water soluble components of the topical composition in the water to form an aqueous solution, and separately mixing emulsifiers into the hydrophobic component of the topical composition. The mixture of the hydrophobic component and surfactant is heated. The aqueous solution is gradually added to the mixture of the hydrophobic component and surfactant while agitating the mixture to form a water-in-oil emulsion. As the concentration of the aqueous solution

in the mixture increases, the emulsion inverts from a water-in-oil emulsion to an oil-in-water emulsion.

According to another aspect of the present invention, the topical composition is disposed on a sheet to form a wet wipe product. Woven or non-woven sheets of the types known to be useful for forming wet wipes are useful in the wet wipe product of the present invention. The sheet is impregnated or wetted with the topical composition of the present invention to form the wet wipe product.

In another aspect of the invention, the topical composition is applied in a thin layer to skin, the water evaporated from the topical composition, and the antimicrobial component or components released onto the skin. The topical composition can be applied to skin directly, such as in a spray, or by way of a wet wipe including the topical composition.

Alternatively, the topical composition can be rinsed from the skin soon after application thereof, in which case the topical composition is used similar to the manner in which soaps are used.

Other features and advantages of the present invention will become apparent to those of ordinary skill in the art through a consideration of the ensuing description and the appended claims.

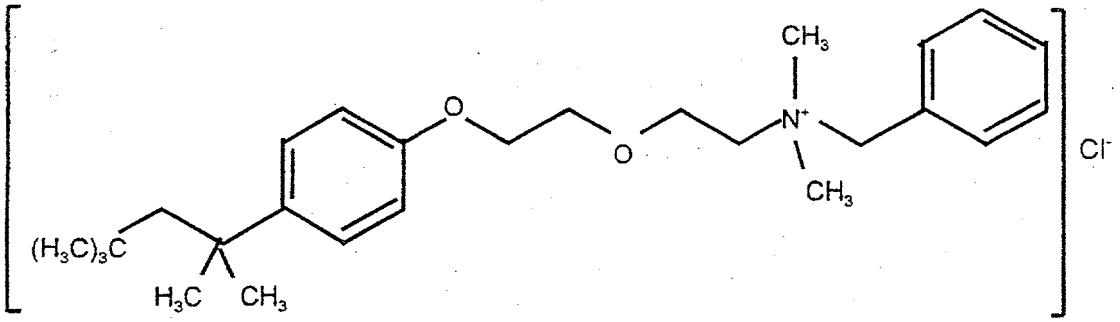
BEST MODE(S) FOR CARRYING OUT THE INVENTION

According to one aspect, the present invention includes an antimicrobial topical composition with an antimicrobial component including a quaternary ammonium compound in a stable emulsion of water and oil. The oil is suspended in the water with at least one cationic surfactant. The antimicrobial topical composition of the present invention is substantially free of low molecular weight alcohols.

Preferably, the antimicrobial component of the topical composition includes a sufficient amount of the quaternary ammonium compound that, when diluted to a 1% solution, the quaternary ammonium compound will kill microorganisms such as *E. coli*, *Staphylococcus* species, and *Pseudomonas* species, as well as viruses such as herpes simplex viruses and rhinoviruses, or at least hold these microorganisms at stasis, thereby preventing a significant increase in the number of microorganisms exposed to the 1% solution and, thus, decreasing the likelihood of infection by microorganisms as

a result of their presence on skin. For example, the quaternary ammonium compound employed as the antimicrobial component of the topical composition of the present invention can constitute up to about 1% of the weight of the topical composition. Preferably, the quaternary ammonium compound of the antimicrobial component makes up from about 0.1% to about 0.2% of the weight of the topical composition.

The antimicrobial component of the topical composition preferably includes the quaternary ammonium compound known in the art as benzethonium chloride, which has the chemical formula:



The antimicrobial activity of benzethonium chloride is noted in Federal Register, Vol. 56. No. 140, Monday, July 22, 1991, 33672-80, the disclosure of which is hereby incorporated by this reference in its entirety. Of course, topical compositions that include another quaternary ammonium compound as the antimicrobial component thereof are also within the scope of the present invention.

The hydrophobic component of the topical composition of the present invention can include hydrophobic, or oil-based, materials, such as oil-based fragrances, oil-based botanical extracts, and hydrophobic materials that moisturize, protect, or otherwise therapeutically benefit the skin.

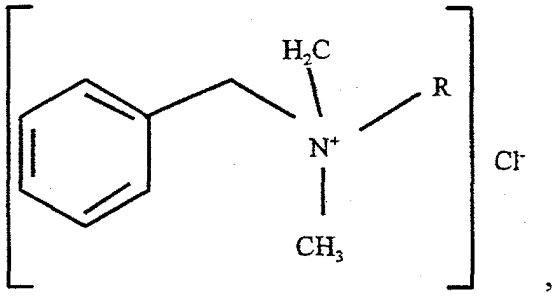
Examples of hydrophobic materials that moisturize, protect, or otherwise therapeutically benefit the skin include, but are not limited to, silicone oils, mineral oils, petrolatum, and long chain, or high molecular weight, alcohols (i.e., alcohols having more than four carbon atoms), such as cetearyl alcohol.

In order to emulsify, or suspend, the hydrophobic (i.e., "water hating") components of the topical composition in the water, or aqueous, portion of the topical composition, the topical composition also includes one or more surfactants. Preferably,

the surfactants used in the topical composition are present in amounts that will not irritate external tissues of the body, such as skin, with prolonged or frequent use.

The surfactants used in the topical composition are preferably cationic surfactants. This is because cationic surfactants are more compatible than other types of surfactants with the quaternary ammonium compound of the antimicrobial component of the topical composition and are, therefore, less likely than other types of surfactants to interfere with the antimicrobial activity or other properties of the quaternary ammonium compounds.

Exemplary cationic surfactants that may be used in the topical composition are quaternary ammonium compounds. One such class of quaternary ammonium compounds is benzalkonium chloride, which has the general formula:



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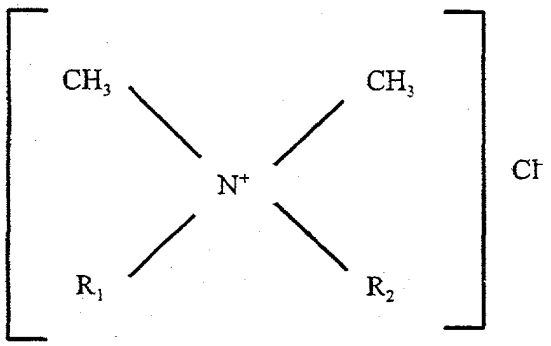
Other quaternary ammonium compounds that may be used in the cationic surfactant component of the topical composition of the present invention include, without limitation, didecyldimethyl ammonium chloride (DDAC), dioctyldimethyl ammonium chloride (DOAC), and octyldecyldimethyl ammonium chloride (DODAC). Generally, quaternary ammonium compounds that are useful in the cationic surfactant component of the topical composition have the chemical formula:



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where R_1 and R_2 both include alkyl groups, R_1 and R_2 both include benzyl groups, or one of R_1 and R_2 includes a benzyl group and the other of R_1 and R_2 includes an alkyl group. When quaternary ammonium compounds are used in the topical composition as cationic surfactants, the quaternary ammonium compounds preferably comprise up to about 1% to about 2% of the weight of the topical composition. More preferably, quaternary ammonium compounds that are employed in the topical composition as cationic surfactants collectively constitute about 0.1% to about 0.5% or about 0.1% to about 1% of the weight of the topical composition. Behentrimonium methosulfate is an example of another surfactant that can be used in the topical composition of the present invention.

The topical composition may also include a preservative component with one or more preservatives. Preferably, the topical composition includes a blend of two or more preservatives. As is known to those of skill in the art, preservatives prevent the growth of microorganisms, such as bacteria, molds, and fungi. A blend of preservatives can facilitate a broader spectrum of activity if the preservatives of the blend prevent the growth of different microorganisms. Combinations of preservatives may also be capable of preventing the growth of microorganisms against which the individual preservatives may not be effective. In addition, in some cases, the total amount of one or more preservatives in the blend can be reduced without reducing the level of activity of those preservatives. Finally, due to the presence of multiple preservatives, the targeted microorganisms are less likely to develop resistance to any one of the preservatives in the blend. For these reasons, it can be said that, in the topical composition of the present invention, certain blends of preservatives are synergistic.

In one embodiment of the topical composition of the present invention, the preferred combination of preservatives includes a one or more parabens. The parabens prevent or control the growth of bacterial microorganisms. Exemplary parabens that can be used in the topical composition include, but are not limited to, methylparabens, ethylparabens, propylparabens, and butylparabens. Preferably, the topical composition of the present invention includes methylparaben and propylparaben. Another exemplary preservative that may be employed in the topical composition of the present invention is a mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one. Potassium sorbate and other sorbic acid preservatives are examples

of other preservatives that can be used in the topical composition. Topical compositions that include other preservatives and other mixtures of preservatives are also within the scope of the present invention.

The topical composition may also include other components, such as fragrances, botanical extracts, pH adjusting agents, or antimicrobial agents. Fragrances may be added to enhance the appeal of the product to consumers. The fragrances can be water soluble or oil-based. Botanical extracts, including both water soluble and hydrophobic materials, may be added to enhance the appeal of the product to consumers, impart a softer feel to the product, or help build healthier skin.

The pH of the formulation can be controlled to avoid irritation to the user's skin, extend shelf-life, and generally enhance the product. Without pH adjusting agents, the pH of the topical composition may change over time, especially if there are long periods of time between manufacture and use of the product.

It is preferable to control or maintain the pH of the topical composition of the present invention. The pH of the topical composition is preferably from about 4 to about 8, and more preferably from about 5 to about 7. By maintaining the pH of the topical composition at such levels, irritation to the user's skin can be avoided, the shelf life of the topical composition can be maximized, and the quality of the topical composition can generally be optimized.

Accordingly, the topical composition of the present invention preferably includes a pH adjusting agent. Preferably, the pH adjusting agent used in the topical composition does not irritate or have any other substantial adverse effects on skin. Exemplary pH adjusting agents that can be used in the topical composition include, but are not limited to, acids, such as sorbic acid, citric acid, or benzoic acid, bases, and known buffers. In addition, the salts of weak acids, amines, or any agent capable of adjusting pH without adversely affecting the skin can be used to regulate the pH of the topical composition of the invention.

According to another aspect of the present invention, some components of the topical composition can serve dual roles. For example, and not to limit the scope of the present invention, potassium sorbate could be used in the topical composition as both a pH adjusting agent and as a preservative.

One embodiment of the topical composition of the present invention is a stable, creamy emulsion that includes moisturizers and emollients. Hydrophilic moisturizers or emollients, such as glycerol, or hydrophobic moisturizers or emollients, such as silicone oils, mineral oils, and petrolatum, can be used in the topical composition.

The following EXAMPLE illustrates, by way of example and not by way of limitation, a specific formulation of the stable, creamy emulsion embodiment of the topical composition of the present invention:

EXAMPLE 1

Component	**Percent (%) of Composition, by Weight**
Water	82.5854
Benzethonium chloride	0.2000
Glycerine	4.9336
Propylene Glycol	0.5526
Cetearyl Alcohol	2.8595
Mineral Oil	4.6672
Petrolatum	1.9735
Dimethicone	0.1776
Fragrances and Botanical Extracts	0.5920
Benzalkonium chloride	0.0900
Behentrimonium methosulfate	1.2255
methylparaben	0.1085
propylparaben	0.0296
5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one	0.0010
Aloe Vera Extract	0.0020
Sea Kelp Extract	0.0010
Apricot Extract	0.0010

If the proportions of the hydrophobic materials and other components of the topical composition are too large, some of these components can diminish or inhibit the antimicrobial activity of the quaternary ammonium compound (e.g., benzethonium chloride) used in the antimicrobial component of the topical composition. Accordingly, the stable, creamy emulsion embodiment of the topical composition of the present invention preferably includes hydrophobic materials and other components in proportions that will not significantly diminish the antimicrobial properties of the antimicrobial quaternary ammonium compound (e.g., benzethonium chloride) of the topical composition. Preferably, hydrophobic materials make up less than about 20% of the weight of the topical composition. More preferably, the topical composition has less than about 17% hydrophobic materials, by weight. Topical compositions that include less than about 15% hydrophobic materials, by weight, are even more preferred.

Stable, creamy emulsions with these proportions of hydrophobic materials can be manufactured in accordance with the hereinafter described method, in which the water soluble components of the topical composition, such as the quaternary ammonium compound of the antimicrobial component, are mixed in the water to form an aqueous solution, and the cationic surfactants, or emulsifiers, are separately mixed into the hydrophobic component of the topical composition.

The mixture of the hydrophobic component and surfactant is heated to facilitate the formation of an emulsion of the desired consistency. Preferably, the hydrophobic component and surfactant mixture is heated to a temperature of about 60° C. to about 100° C. Temperatures in the range of about 70° C. to about 90° C. are more preferred. As an example, the aqueous solution may be heated to a temperature of about 75° C. to about 80° C. while being mixed, while the hydrophobic component and surfactant mixture may be heated to a temperature of about 85° C. to about 90° C. while being mixed. Components of the topical composition that are sensitive to heat may be left out of the aqueous solution, the hydrophobic component, or the mixture until after the emulsion is cooled to a temperature that will not affect the activities of these heat-sensitive components.

While the hydrophobic component and surfactant mixture is maintained at a substantially constant temperature, the aqueous solution is gradually added to the mixture with sufficient agitation to form small droplets of the aqueous solution in the

hydrophobic component and, thus, to form a water-in-oil emulsion. The water-in-oil emulsion is preferably maintained at an increased temperature while the aqueous solution is mixed therein.

As the concentration of the aqueous solution in the emulsion increases, the emulsion inverts from a water-in-oil emulsion to an oil-in-water emulsion. Once the emulsion becomes an oil-in-water emulsion, the remainder of the aqueous solution can be added to the emulsion at an increased rate until the desired proportions of aqueous solution and hydrophobic components have been obtained. Mixing of the emulsion may be continued as the temperature thereof is decreased to a gel point of the emulsion and to cooler temperatures.

Of course, other techniques known in the art may also be used to make a stable, creamy emulsion incorporating teachings of the present invention.

An exemplary hand-wash formulation of an antimicrobial topical composition incorporating teachings of the present invention is illustrated in the following EXAMPLE:

EXAMPLE 2

Component	**Percent (%) of Composition, by Weight**
Water	85.994
Benzethonium chloride	0.200
MAQUAT CETAC-30% (Mason)	0.500
Benzalkonium chloride	0.113
Glycerine	1.000
Petrolatum	1.973
INCROQUAT BTMS (Croda)	4.085
Mineral Oil	4.667
Dimethicone	0.178
Fragrances and Botanical Extracts	0.304
GERMABEN II	0.987

KATHON (Isocil PC)	
methylparaben	0.1085
propylparaben	0.0296
5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one	0.0010
Aloe Vera Extract	0.0020
Sea Kelp Extract	0.0010
Apricot Extract	0.0010

In still another embodiment, the topical composition of the present invention is a more dilute, liquid emulsion that includes a small proportion of hydrophobic components. This liquid embodiment of the topical composition may have about 95% or more water, by weight. The following EXAMPLE illustrates, by way of example and not by way of limitation, a specific formulation of a liquid, or less viscous, embodiment of the topical composition of the present invention:

EXAMPLE 3

Component	**Percent (%) of Composition, by Weight**
Water	97.4616
Benzethonium chloride	0.2000
Jojoba PEG80	1.0000
Polyethylene Glycol 400	0.8700
Propylene Glycol	0.0230
Cocomide Betaine	0.2000
Fragrances and Botanical Extracts	0.0820
Cocophosphatidyl-PG-dimonium chloride	0.0410
Benzalkonium chloride	0.0900
Polysorbate 80	0.0064
diazolidinyl urea	0.0120

methylparaben	0.0045
propylparaben	0.0012
5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one	0.0009
Squalene	0.0041
Aloe Vera Extract	0.0021
Sea Kelp Extract	0.0006
Apricot Extract	0.0006

The less viscous embodiments of the topical composition can be manufactured by known processes or by employing the method described above in reference to the manufacture of the stable, creamy emulsion embodiment of the topical composition, then further diluting the composition to the desired consistency.

Of course, some of the less viscous embodiments of the topical composition of the present invention need not include any hydrophobic components.

As an example of the use of topical compositions incorporating teachings of the present invention, including the stable, creamy emulsion embodiments, as well as the less viscous embodiments, the topical composition may be rubbed onto to skin (e.g., on hands). When kept in contact with the skin for at least about ten or fifteen seconds, the topical composition of the present invention eliminates many microorganisms, including bacteria and some viruses.

The topical composition can be left on the skin, wherein water evaporates from the skin and the remaining components of the topical composition, such as antimicrobial component, the hydrophobic components, and the surfactants remain on the skin or are absorbed into the skin. When left on the skin, the topical composition demonstrates prolonged activity against some microorganisms. For example, when left on the skin, the topical composition remains active against *Staphylococcus aureus* for as long as four hours or more. In one study wherein the topical composition was left on skin, at four hours after application of the topical composition to the skin the number of *S. aureus* on the skin was about 98.8% less than the number of *S. aureus* on the skin prior to application of the topical composition. As another example, the topical

composition remains effective against *E. coli* for at least about two hours. After fifteen seconds, the topical composition reduces the number of *E. coli* by about 99.999%. At ten minutes following application of the topical composition, the number of *E. coli* increased, but remained at about 55.3% less than the number of *E. coli* prior to application of the topical composition. After two hours, the number of *E. coli* on the skin was still about 36.9% less than the number of *E. coli* prior to application of the topical composition.

Alternatively, after applying the topical composition to the skin, the topical composition can be removed from the skin, such as by rinsing with water (i.e., used similarly to a soap). When rinsed from skin, a topical composition with less than about 20%, by weight, hydrophobic components does not leave a tacky or oily residue on the skin, as may occur with many conventional creamy emulsions that have higher proportions of hydrophobic components.

Topical compositions incorporating teachings of the present invention are also effective in reducing populations of *Mycobacterium Bovis*, which causes tuberculosis. When *Mycobacterium Bovis* is exposed to an exemplary topical composition incorporating teachings of the present invention, the population of *Mycobacterium Bovis* is reduced by about 96.3%. When the exposure time is increased to about 30 seconds, the number of *Mycobacterium Bovis* bacteria is reduced by about 97.4%.

Topical compositions incorporating teachings of the present invention may also have antiviral activities. These antiviral activities may be exhibited with long exposure times, as well as with relatively short exposure times, such as when the topical composition is applied to the skin and, shortly thereafter, removed from the skin. Topical compositions according to the present invention may also kill viruses when left on the skin for longer periods of time. The following TABLE includes examples of viruses against which the topical composition of EXAMPLE 2, as well as other embodiments of topical compositions incorporating teachings of the present invention, is effective. As shown in the following TABLE, the topical compositions of the present invention may reduce the number of viruses significantly, such as by greater than about 99%, in exposure times as short as about 15 seconds or less.

TABLE

		IN-VITRO TIME KILL	
VIRUS	Type	Exposure Time	Percent Reduction
Herpes Simplex Virus	Type 1	15 seconds	99.7%
		30 seconds	99.98%
		60 seconds	99.8%
Human Immunodeficiency Virus (HIV)	Type 1	15 seconds	99.9%
		30 seconds	99.94%
		60 seconds	99.99%
Influenza Virus	Type A2	15 seconds	99.94%
		30 seconds	99.94%
		60 seconds	99.98%

According to another aspect of the present invention, the liquid embodiment of the topical composition is disposed on a sheet to form a wet wipe product. Woven or non-woven sheets of the types known to be useful for forming wet wipes are useful in the wet wipe product of the present invention. The sheet is impregnated or wetted with the topical composition of the present invention to form the wet wipe product.

In another aspect of the invention, the liquid embodiment of the topical composition is applied in a thin layer to skin, the water evaporated from the topical composition, and the antimicrobial component released onto the skin. The topical composition can be applied to skin directly, by spraying, or by way of a wet wipe including the liquid topical composition. When left on the skin for about ten or fifteen seconds or more, the liquid embodiment of the topical composition reduces the number of bacteria and virus particles on the skin in a manner similar to that of the creamy emulsion embodiment of the topical composition.

While certain representative embodiments and details have been shown for purposes of illustrating the invention, it will be apparent to those skilled in the art that various changes in the invention disclosed herein may be made without departing from the scope of the invention, which is defined in the appended claims.

CLAIMS

What is claimed is:

1. An antimicrobial topical composition, comprising:

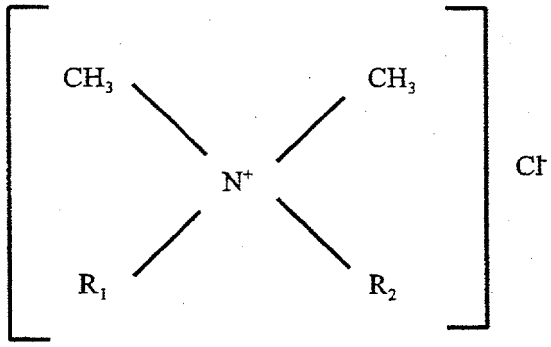
water;

an antimicrobial component comprising benzethonium chloride;

a hydrophobic component; and

a cationic surfactant component for emulsifying said hydrophobic component in said water.

2. The antimicrobial topical composition of claim 1, wherein said cationic surfactant component comprises the general formula:



,

where R_1 and R_2 both comprise alkyl groups, R_1 and R_2 both comprise benzyl groups, or one of R_1 and R_2 comprises a benzyl group and the other of R_1 and R_2 comprises an alkyl group.

3. The antimicrobial topical composition of claim 1, wherein said antimicrobial component comprises less than about 1% of the weight of said antimicrobial topical composition.

4. The antimicrobial topical composition of claim 1, wherein said antimicrobial component comprises about 0.1% to about 0.2% of the weight of said antimicrobial topical composition.

5. The antimicrobial topical composition of claim 1, wherein said cationic surfactant component comprises less than about 1% of the weight of said antimicrobial topical composition.

6. The antimicrobial topical composition of claim 1, comprising about 0.1% to about 0.5% of said cationic surfactant component, by weight.

7. The antimicrobial topical composition of claim 1, further comprising more than one preservative.

8. The antimicrobial topical composition of claim 7, wherein said more than one preservative comprises a synergistic blend of methylparaben and propylparaben.

9. The antimicrobial topical composition of claim 7, wherein:

said hydrophobic component comprises petrolatum, a mineral oil, a silicone oil, or an oil-based fragrance, said hydrophobic component forming a stable, creamy emulsion with said water and comprising less than about 20%, by weight, of the composition;

said cationic surfactant comprises at least one of benzalkonium chloride, didecyldimethyl ammonium chloride, dioctyldimethyl ammonium chloride, and decyloctyldimethyl ammonium chloride; and

at least one of said more than one preservative comprises sorbic acid or a salt thereof, diazolidinyl urea, methylparaben, ethylparaben, propylparaben, butylparaben, or a mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one.

10. The antimicrobial topical composition of claim 9, comprising less than about 15%, by weight, of said hydrophobic component, said hydrophobic component forming a stable, creamy emulsion with said water.

11. The antimicrobial topical composition of claim 1, comprising at least about 95%, by weight, of said water.

12. The antimicrobial topical composition of claim 1, said topical composition being substantially free of low molecular weight alcohols.

13. A wet wipe comprising a sheet wetted with the antimicrobial topical composition of any of claims 4, 10, 11, and 12.

14. A method for reducing a number of microorganisms on a surface, comprising applying to the surface a substantially low molecular weight alcohol-free topical composition with a benzethonium chloride antimicrobial agent, a hydrophobic component, and a cationic surfactant.

15. The method of claim 14, further comprising removing said topical composition from the surface.

16. The method of claim 14, further comprising leaving said topical composition on the surface.

17. A method for manufacturing an antimicrobial topical composition, comprising:

forming a mixture of a cationic surfactant and a hydrophobic component;

heating said mixture;

forming an aqueous solution of water and an antimicrobial component comprising a quaternary ammonium compound;

adding said aqueous solution gradually to said mixture;

agitating said mixture during said adding to form a water-in-oil emulsion;

inverting said water-in-oil emulsion to form an oil-in-water emulsion; and

diluting said oil-in-water emulsion.

18. The method of claim 16, wherein said forming said aqueous solution comprises dissolving benzethonium chloride in said water.

19. The method of claim 16, wherein said forming said mixture comprises mixing at least one cationic surfactant with said hydrophobic component.

20. The method of claim 16, wherein said heating comprises heating said mixture to a temperature of about 60° C. to about 100° C.

21. The method of claim 16, wherein said heating comprises heating said mixture to a temperature of about 70° C. to about 80° C.

22. The method of claim 16, further comprising substantially maintaining a temperature of said water-in-oil emulsion during said adding.

23. The method of claim 16, wherein said diluting comprises adding water to said oil-in-water emulsion to form a stable, creamy emulsion comprising less than about 20%, by weight, of said hydrophobic component.

24. The method of claim 16, wherein said diluting comprises adding water to said oil-in-water emulsion to form a liquid emulsion comprising at least about 95% of said water.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/25853

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 6/00, 7/00, 7/075; A01N 25/34
US CL :424/70.27, 70.28, 402
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/70.27, 70.28, 402

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y,P	US 5,994,383 A (DYER et al) 30 November 1999, col.4, lines 4-7, col.7, line 27, col.10, lines 48-60, col.11, lines 66 and 67, col.12, line 13	1-24
Y	US 5,759,557 A (EPSTEIN et al) 02 June 1998, col.3, lines 5,41-43, col.3, lines 59-61, col.6, lines 20-31, col.6, lines 64-67 and col.7, lines 1-49.	1-24
Y	US 5,705,532 A (MODAK et al) 06 January 1998, col.3, lines 3-17, col.3, line 42, col.3, lines 43-50 and col.3, line 60.	1-24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
19 OCTOBER 2000	24 NOV 2000
Name and mailing address of the ISA/US	Authorized officer